## REMARKS/ARGUMENT

***Claim Amendments***

Claims 1-57 are cancelled without prejudice.

New Claim 58 has been drafted to define the composition of matter more particularly.

New Claim 59 has been drafted to define the composition of matter of claim 58 more particularly, in that the PS divalent metal salt is obtained from lecithin which is not solubilized, in a substantially aqueous reaction system. Support for the amendment may be found, for example, in Example 1.

New claim 60 is added to define the composition of matter of claim 59 more particularly, in that the PS is divalent metal salt is obtained from lecithin which is dispersed in the substantially aqueous reaction system. Support for the amendment may be found, for example, in Example 1.

Remaining new claims are drafted to depend from new claims 58 and/or 59.

New claim 61 is drafted to narrow the range of PS recited in claim 58 to about 1 to about 45% (w/w).

It is respectfully submitted that no new matter has been added.

**Applicant's submissions**

***General***

The present amendment is in response to the Final Office action of March 16, 2010.

Without conceding to any of the Examiner's rejections, this amendment is submitted in order to expedite prosecution of the application.

The new claims have been drafted to the specific embodiment of the invention in which the claimed composition is a dispersion of divalent salt of phosphatidylserine

(PS) in an edible oil base. The divalent salt is in particulate solid form, more particularly one of calcium and magnesium PS salts dispersed in the edible oil base. The PS divalent salt is not soluble in the edible oil base, and is dispersed therein as a solid phase. The oil base may be edible medium-chain triglycerides. Capsules may contain the novel composition. Further various uses of the novel composition are claimed.

***Experimental evidence***

Applicant respectfully submits herewith a declaration by one of the inventors, Gai Ben-Dror. As detailed in the declaration attached hereto, divalent PS salts which are prepared in a diphasic system, are soluble in oils, including edible oils.

As shown by the Gai Ben-Dror declaration, divalent PS salts prepared in various diphasic systems, such as those of De Ferra et al., result in clear solutions when mixed with oils, i.e. they are soluble in oil. It is not possible to prepare dispersions of such divalent salts in oil, because they completely dissolve in the oil, including edible oil, such as, edible medium-chain triglycerides.

The declaration attached hereto is marked Annex A.

***Claim objections***

The new Claims have been drafted in consideration of the Examiner's remarks.

***Claim Rejections – 35 USC § 112***

The Examiner rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 due to the introduction of the definition "predominantly" in the previous Supplementary Amendment. The said definition is absent in the new claims.

The Examiner further rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 due to the definition of the stability being indefinite. The new claims define this element as decomposition of "less than about 5% in at least 6 months".

The Examiner further rejected claims 55-57 and their dependent claims 2, 5, 8, 14-

15, 17, 20-21, 24, 27, 30, 33 and 53-54 as vague and indefinite, due to the definition "nutritional carbohydrates". It is submitted that the term is clear, and encompasses dietary sugars, polysaccharides, starches, fibers, etc. Nonetheless, without conceding to the Examiner's objection, in order to expedite examination, this term has been revised to "carbohydrates" in the new claims.

***Novelty***

Applicants wish to thank the Examiner for having withdrawn the objections of lack of novelty on record.

***Inventive step***

The Examiner rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 under 35 USC § 103(a) as being unpatentable over De Ferra et al. (EP 922707) in view of Jorissen et al. (Nutritional Neuroscience, 2002).

The Examiner maintains that De Ferra et al. teach the preparation of PS and its purification by crystallization in the form of the calcium salt, with reference to Examples 1-3 of De Ferra et al., which exemplify the preparation of a purified PS as the calcium salt, from various lecithin sources.

The Examiner further asserts that De Ferra et al. do not teach the incorporation of the PS in a pharmaceutical composition, but that this deficiency is remedied by Jorissen et al.

According to the Examiner, Jorissen et al. describe the administration of PS, admixed with other phospholipids and polyunsaturated fatty acids, encapsulated in a soft gel capsule.

The Examiner therefore states that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. with those of Jorissen et al. and utilize the purified PS of De Ferra in a pharmaceutical composition, and one of ordinary skill in the art would have been motivated to do so.

With regard to the storage stability, the Examiner states that although De Ferra et al. is silent, since it is known in the art to utilize oils (MCT) for diluting PS, their use is obvious. Therefore, based on the teachings of De Ferra et al. that the divalent salt of PS is the purer form of PS, there is reasonable expectation that the storage stability would be the same as that instantly claimed.

Applicants respectfully traverse.

De Ferra et al. teach the preparation of PS, and its purification by crystallization as the calcium salt, in a diphasic system using as starting material lecithin which was dissolved in the organic phase. As proven by clear evidence in applicant's attached experimental evidence (Declaration by inventor Gai Ben-Dror, hereafter "the Declaration"), PS calcium salts produced in diphasic systems from lecithin that is dissolved in the organic phase, such as those taught by De Ferra et al., are soluble in oils, therefore a dispersion of solid particles of PS calcium cannot be made. See the evidence presented in Section I of the Declaration, wherein Example 2 of De Ferra et al. was repeated, and the resulting product dissolved in the MCT with which it was mixed to give a **clear** PS solution, proving that the PS calcium salt thus obtained is soluble in edible MCT oil. The additional example in the Declaration (Section 2), constitutes evidence that proves that producing PS in a diphasic reaction where the starting material lecithin is dissolved in the organic phase, results in a clear fluid vegetable oil containing soluble PS calcium salt. This proves that the diphasic reaction only produces a divalent salt (Ca) of PS that is soluble in oil.

As defined in claim 58 the PS composition of matter of the invention is an edible oil containing a **dispersion** of a divalent metal salt of PS, not a solution of PS in the oil, because the PS salt is insoluble in said oil. This is a major difference, which highly influences the stability of the PS as proven by the evidence submitted.

In a PS dispersion, it is suggested that molecules on the surface of the dispersed particles are exposed to the surrounding medium (in the present case the oil base) while molecules in the inner part of the dispersed particles are much less exposed to the medium and thus exhibit high stability, whereas on the other hand, in a PS oil

solution, of oil-soluble PS salts as described in the prior art, there are no protected "particles", and thus, the molecules, being dissolved, are exposed completely to the oil environment and have high decomposition rates.

As proven by the declaration by Neta Scheinman, oil dispersions of the PS divalent metal salts prepared as described in the specification, which are insoluble in the oil, were considerably more stable at long storage and under extreme conditions than conventional solutions of PS.

With particular reference to Jorissen et al., it is respectfully submitted that one of ordinary skill in the art would not have been motivated to combine the teachings of De Ferra with this document, because it is clearly stated that: "*In that article (an earlier work by Jorissen et al.) we concluded that future studies should focus on the way of production of S-PS (soy-PS), because in our studies the S-PS content of the capsules degraded to 50% of the initial value after 15 months*." (see page 342, penultimate paragraph). The Jorissen et al. reference cited by the Examiner is a mere safety study, and does not remedy the basic art deficiency, because conventional production of S-PS is described. The Examiner assumes that the purified PS obtained by the process of De Ferra et al. should be stable. This assumption is not supported, by any evidence. Even if one were to adopt such assumption, since Jorissen et al. clearly describe the instability of S-PS, which was in *pure* form (see page 338, right hand column, "Treatment"), one of ordinary skill in the art would have been taught away from using the pure PS of De Ferra, mixed with oils and encapsulated in a gelatin capsule as in Jorissen, because clearly the PS content would have dissolved in the oils and would have been substantially degraded. Reference is made to the declaration by Dr. Neta Scheinman, submitted together with the former Amendment, which proved the novelty and high storage stability of the PS salt dispersions of the invention, particularly when encapsulated in gelatin capsules.

As to the method claims, the advantages of the PS composition of the invention have been demonstrated during the prosecution of this invention in the past, and above. Therefore, the method is of the invention, employing the inventive compositions of matter, food articles and pharmaceutical compositions are also advantageous, ensuring

that a patient receives an effective dose of the PS, which cannot be ensured using the degradable compositions of Jorissen, in which the dose is constantly diminished due to degradation and in thus ineffective.

The same arguments apply to new claims 58 and 59.

It is therefore respectfully submitted that the claimed invention is unobvious under 35USC 103 and potentially distinguishable over De Ferra et al. (EP 922707) in view of Jorissen et al. (Nutritional Neuroscience, 2002).

The Examiner further rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, and 53-57 under 35 USC § 103(a) as being unpatentable over De Ferra et al. (EP 922707) in view of Douglas Laboratories (1999).

De Ferra was addressed by the Examiner as above.

With regard to Douglas Laboratories, the Examiner maintains that this document, which is a data sheet for a dietary supplement discloses a softgel which contains a mixture of phospholipids, inter alia PS, and fatty acids, and also other ingredients such as MCT and soy bean oil. The softgel capsules are designed for supporting the body's nervous system and brain function.

The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. and of Douglas Laboratories and utilize the purified PS in the pharmaceutical composition of Douglas Laboratories, and one of ordinary skill in the art would have been motivated to do so.

Applicants respectfully traverse.

For the same arguments presented above, the Examiner's conclusion that using the salts of De Ferra in preparing capsules according to Douglas Laboratories would result in encapsulated PS as claimed in the present invention is not sustainable. The fact that

a salt is pure does not ensure its properties. The salts of De Ferra being soluble in oil would have dissolved in the medium, as explained above in respect of Jorissen.

The Examiner further rejected also claims 30 and 33 as being unpatentable over De Ferra et al. in view of Douglas Laboratories and further in view of Geiss (US PGPUB 20040120985).

De Ferra et al. and Douglas Laboratories were addressed as above. With regard to Geiss, the Examiner holds that this document teaches that administration of PS protects against neurons atrophy, normalizes cholesterol/phospholipids ratio in the aging brain, etc.

The Examiner therefore concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. in view of Douglas Laboratories and Geiss, and use the PS supplement in a method of enhancing cognitive performance and learning ability as well as improving age-related memory loss, and that the man of ordinary skill in the art would have been motivated to do so.

Applicants respectfully traverse, for all of the reasons detailed above.

***Double Patenting***

Applicants wish to thank the Examiner for having withdrawn the earlier objections.

In light of the foregoing remarks, it is respectfully solicited that the new claims presented herewith be favorably considered as placing the application in condition for allowance. Early passage of this case to issue is earnestly requested. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time, time sufficient, to effect a timely

response, and shortages in this or other fees, be charged, or any overpayment in fees be credited, to the Deposit Account of the undersigned, Account No. 500601 (Docket no. 7056-X08-020).

Respectfully submitted,

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Attachment: Declaration with Annex A